Notice of Allowability	Application No.	Applicant(s)	
	10/061,438	MCCROSKEY ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *May 18, 2006*.

2. ☒ The allowed claim(s) is/are *41-52, 54 and 56-69 (renumbered 1-27, respectively)*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date 08/11/06
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Ned Israelsen on August 9, 2006.

In the Specification:

Please replace the title of the invention with the following:

RATIOMETRIC DETERMINATION OF GLYCATED PROTEIN

Please replace the abstract with the following rewritten abstract:

The present invention provides methods for determining a ratio of glycated to total protein in samples containing glycated proteins, glycosylated proteins, or glycoproteins. The method incorporates lateral flow test strip or vertical flow test strip devices having negatively charged carboxyl or carboxylate groups and hydroxyboryl groups immobilized and interspersed on a solid support matrix. The solid support matrix may include derivatives of cellulose (*e.g.*, carboxy cellulose) derivatized with carboxylic acid (*e.g.*, carboxylate, carboxyl) groups and hydroxyboryl compounds including phenylboronic acid (*i.e.*, phenylborate), aminophenylboronic acid, boric acid (*i.e.*, borate), or other boronic acid (*i.e.*, boronate) compounds. The present invention is useful for monitoring glycation

or glycosylation of hemoglobin or albumin for monitoring glycemic control (*e.g.*, glycemia) in diabetes.

On page 17, line 13, please delete the word "polyacrylande" and replace with "polyacrylamide".

On page 17, line 15, please delete the word "destran" and replace with "dextran".

On page 17, line 17, please delete the word "polystyrenes" and replace with "polystyrenes".

On page 31, lines 1-2, please amend the sentence as follows:

The resulting samples were assayed in accordance with the present invention as described in Example 2, and the A280 absorbance values recorded ~~above~~ in Table IV.

On page 32, line 7, please delete the number "5" and replace with "2".

In the Claims:

Please cancel Claims 53 and 55.

Please amend Claims 41, 49 and 54 as follows:

41. (Examiner's Amendment) A method for ~~measuring~~ determining a ratio of glycated ~~and nonglycated forms of a~~ to total protein in a sample~~, wherein the sample contains~~ containing both glycated and nonglycated ~~forms of the~~ protein, comprising:

providing a solid support having negatively charged carboxyl groups immobilized thereon, which groups are capable of binding both ~~the~~ glycated and ~~the~~ nonglycated ~~forms of the~~ protein at a first pH, said support also having hydroxyboryl groups immobilized thereon, interspersed with the negatively charged carboxyl groups, which hydroxyboryl groups are capable of binding ~~the~~ glycated ~~form of the~~ protein at a second pH;

adding the sample to the solid support at the first pH, thereby binding both ~~the~~ glycated ~~protein~~ and ~~the~~ nonglycated protein to the negatively charged carboxyl groups on the solid support, ~~at the first pH~~ and then performing a first measurement indicative of the ~~amount of glycated and nonglycated forms of the~~ total protein bound to the solid support; ~~and~~

changing the pH on the support to the second pH, thereby removing both the nonglycated protein and the glycated protein from the negatively charged carboxyl groups, after which removal the glycated protein immediately binds to the hydroxyboryl groups on the support independent of incubation time, and then performing a second measurement indicative of the amount of the glycated protein bound to the solid support; and

determining the ratio of glycated to total protein in the sample from the first and second measurements.

49. (Examiner's Amendment) The method of Claim 41, wherein the first and second measurements measure ~~a physical~~ an optical property of the protein.

54. (Examiner's Amendment) The method of Claim 41, wherein the solid support ~~matrix~~ is selected from the group consisting of cellulose, nitrocellulose, cellulose acetate, polyacrylamide, agarose polyacrylamide copolymer, agarose, starch, nylon, nylon polyesters, dextran, cross-linked dextran, dextran acrylamide copolymer, cross-linked hydroxyethylmethacrylate, substituted cross-linked polystyrenes, polyvinylalcohol, wool, metal oxides, porous ceramics coated with hydrophilic organic polymers and glass.

Please add new Claims 56-69 as follows:

56. (New) A method for determining a ratio of glycated albumin to total protein in a sample containing both glycated and nonglycated protein, comprising:

providing a strip-type device comprising:

(1) a solid support matrix having a measurement area; and

(2) negatively charged carboxyl groups and dihydroxyboryl groups immobilized and interspersed on the solid support matrix, said negatively charged carboxyl groups are capable of binding both glycated and nonglycated protein at a first pH between about 5.0 and about 7.0, and said dihydroxyboryl groups are capable of binding glycated protein at a second pH between about 8.0 and about 10.0;

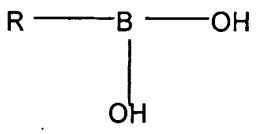
adding the sample to the solid support matrix at the first pH, thereby binding both glycated and nonglycated protein to the negatively charged carboxyl groups on the solid support matrix, and then performing a first optical

measurement on the measurement area indicative of the total protein bound to the solid support matrix;

changing the pH on the solid support matrix to the second pH, thereby removing both the nonglycated protein and the glycated protein from the negatively charged carboxyl groups, after which removal the glycated protein immediately binds to the dihydroxyboryl groups on the solid support matrix independent of incubation time, and then performing a second optical measurement on the measurement area indicative of the amount of glycated albumin bound to the solid support matrix; and

determining the ratio of glycated albumin to total protein in the sample from the first and second optical measurements.

57. (New) The method of Claim 56, wherein said dihydroxyboryl groups have the formula:



where R is selected from the group consisting of phenyl, alkyl of 1-6 carbons, ethyl, 1-propyl, 3-methyl-1-butyl and aminophenyl.

58. (New) The method of Claim 56, wherein the solid support matrix is selected from the group consisting of cellulose, nitrocellulose, cellulose acetate, polyacrylamide, agarose polyacrylamide copolymer, agarose, starch, nylon, nylon polyesters, dextran, cross-linked

dextran, dextran acrylamide copolymer, cross-linked hydroxyethylmethacrylate, substituted cross-linked polystyrenes, polyvinylalcohol, wool, metal oxides, porous ceramics coated with hydrophilic organic polymers and glass.

59. (New) The method of Claim 58, wherein said solid support matrix is carboxy cellulose.

60. (New) The method of Claim 56, wherein said first pH is achieved with a buffer selected from the group consisting of MES, MOPS and HEPES.

61. (New) The method of Claim 56, wherein said second pH is achieved with a buffer selected from the group consisting of ammonium acetate or taurine.

62. (New) The method of Claim 56, wherein the sample comprises blood, plasma or serum.

63. (New) A method for determining a ratio of glycated hemoglobin to total protein in a sample containing both glycated and nonglycated protein, comprising:

providing a strip-type device comprising:

(1) a solid support matrix having a measurement area; and

(2) negatively charged carboxyl groups and dihydroxyboryl groups immobilized and interspersed on the solid support matrix, said negatively charged carboxyl groups are capable of binding both glycated and nonglycated protein at a first pH between

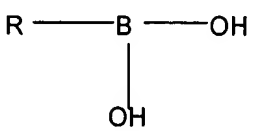
about 5.0 and about 7.0, and said dihydroxyboryl groups are capable of binding glycated protein at a second pH between about 8.0 and about 10.0;

adding the sample to the solid support matrix at the first pH, thereby binding both glycated and nonglycated protein to the negatively charged carboxyl groups on the solid support matrix, and then performing a first optical measurement on the measurement area indicative of the total protein bound to the solid support matrix;

changing the pH on the solid support matrix to the second pH, thereby removing both the nonglycated protein and the glycated protein from the negatively charged carboxyl groups, after which removal the glycated protein immediately binds to the dihydroxyboryl groups on the solid support matrix independent of incubation time, and then performing a second optical measurement on the measurement area indicative of the amount of glycated protein bound to the solid support matrix; and

determining the ratio of glycated hemoglobin to total protein in the sample from the first and second optical measurements.

64. (New) The method of Claim 63, wherein said dihydroxyboryl groups have the formula:



where R is selected from the group consisting of phenyl, alkyl of 1-6 carbons, ethyl, 1-propyl, 3-methyl-1-butyl and aminophenyl.

65. (New) The method of Claim 63, wherein the solid support matrix is selected from the group consisting of cellulose, nitrocellulose, cellulose acetate, polyacrylamide, agarose polyacrylamide copolymer, agarose, starch, nylon, nylon polyesters, dextran, cross-linked dextran, dextran acrylamide copolymer, cross-linked hydroxyethylmethacrylate, substituted cross-linked polystyrenes, polyvinylalcohol, wool, metal oxides, porous ceramics coated with hydrophilic organic polymers and glass.

66. (New) The method of Claim 63, wherein said solid support matrix is carboxy cellulose.

67. (New) The method of Claim 63, wherein said first pH is achieved with a buffer selected from the group consisting of MES, MOPS and HEPES.

68. (New) The method of Claim 63, wherein said second pH is achieved with a buffer selected from the group consisting of ammonium acetate or taurine.

69. (New) The method of Claim 63, wherein the sample comprises blood, plasma or serum.

Election/Restrictions

Claims 41-52 and 54 are generic and allowable. Herein, Examiner withdraws the restriction requirement of October 6, 2004, with respect to species claims of Group II, claims 22-34 (cancelled in Applicants' reply, filed December 8, 2005).

In view of the above withdrawal of the restriction requirement, Applicants are advised that any claims presented in a future continuation application or divisional application that include all the limitations of the allowable generic linking claims may be subject to statutory or nonstatutory double patenting rejections over the claims of the instant application. Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Conclusion

Claims 41-52 and 54 are allowed.

Claims 53 and 55 are cancelled by Examiner's Amendment.

Claims 41, 49 and 54 are amended by Examiner's Amendment.

The Restriction requirement of October 6, 2004, is withdrawn. New Claims 56-69 are added by Examiner's Amendment to capture originally presented species claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600